UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,851	11/20/2001	Rachel E. Meyers	10147-56U1	1565

7590 01/03/2005

Intellectual Property Group
MILLENNIUM PHARMACEUTICALS, INC.
75 Sidney Street
Cambridge, MA 02139

EXAMINER	
SCHULTZ, JAMES	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 01/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/001,851	MEYERS ET AL.	
	Examiner	Art Unit	
	J. D. Schultz, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27,29-31 and 36-60* is/are pending in the application.

4a) Of the above claim(s) *43-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27,29-31 and 36-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/12/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed October 12, 2004 has been considered. Rejections and/or objections not reiterated from the previous office action mailed February 13, 2004 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code, at page 12 for example. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Election/Restrictions

Newly submitted claims 43-60 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The new claims are directed to an invention that is unrelated to the originally examined claims. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are different because the originally examined claims relate to methods of screening compounds that modulate tumorigenesis comprising measuring the effect

of a candidate compound on activity of SEQ ID NO: 2. The newly submitted claims 43-60 are drawn to methods of assaying for compounds that bind to SEQ ID NO: 2. Because the steps and techniques of measuring activity of SEQ ID NO: 2 are different from those assays that detect binding and thus have different modes of operation, and because the two methods are not disclosed as capable of use together, restriction is considered proper. Furthermore, because a search for methods of using assays that measure binding, such as competitive binding assays, or yeast two hybrid screens, is not expected to overlap with methods of measuring glycosyl transferase activity, a serious burden exists to search and examine these inventions in the same application. Restriction is considered proper therefore.

Since applicant has received an action on the merits for the originally presented invention of claims 27, 29-31, and 36-42, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 43-60 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Response to Claim Rejections - 35 USC § 112

Claims 27, and 29-31, and new claims 36-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and is repeated for the same reasons of record as cited in the action mailed February 13, 2004.

At the outset it is noted that applicants have amended the claims such that the method does not seek modulators of SEQ ID NO: 2 *per se*, but rather seeks methods of screening for modulators of tumorigenesis comprising the use of test compounds on compositions which comprise SEQ ID NO: 2, with no requirement that the composition impact SEQ ID NO: 2 in any way. While a role for SEQ ID NO: 2 in this process has not been claimed, all rejections made under 35 U.S.C. § 112 first paragraph in this action presume, based on the previous claim language which sought modulators of SEQ ID NO: 2, that the method seeks modulators of SEQ ID NO: 2 in a process of screening for modulators of tumorigenesis. This is not true in regards to the rejection under 35 U.S.C. § 102(b) provided below. In this rejection a literal reading of the claims are made, whereby the invention is considered to be a method of screening for modulators of tumorigenesis wherein only the presence of SEQ ID NO: 2 is required, but not for any claimed purpose.

Applicants' amendment and arguments filed 10 September 2004 have been fully considered. Applicants' amendment and arguments as they pertain to use of sequences with 95% homology to SEQ ID NO: 2 are considered convincing. The specification is considered to teach domains that would provide one of skill with the knowledge needed to change the sequence within the 5% change allowed and still retain a functional protein. However, these arguments are not considered to be convincing as they pertain to the use of nucleotides that are at least 100 amino acids long that retain glycosyl transferase activity. This is because, as stated in the action mailed February 13, 2004, one of skill could not use the teachings of the specification that relate to active domains to understand which 100 amino acid fragments would retain the claimed activity. This is because the genus of fragments is considerably larger than the genus of

sequences that are 95% identical to SEQ ID NO: 2, and applicants are not considered to have provided a representative sample of the large genus of any amino acid fragment 100 amino acids or longer that retain glycosyl transferase activity such that one of skill in the art would be convinced applicants were in possession of the genus as claimed.

While applicants point to one fragment that has more than 100 amino acids and retains glycosyl transferase activity, this is not considered to be representative of all such fragments such that one could understand which undisclosed fragments would have the claimed activity. Applicants have additionally pointed to conservative amino acid substitutions as a mechanism for generating fragments that retain the claimed activity. While such substitutions are well known in the art, this is not considered to convey the specific knowledge one of skill would require in order to make any particular fragment that retains glycosyl activity, because it is well known in the art that substitution of even a single amino acid can have unforeseen consequences on protein folding and activity. For example, Bloom et al. teaches that single point mutations within a gene related to a rare disorder can eliminate ATPase and DNA helicase activities (Oncology. 1998. Vol. 17, 2565-2571). The disclosure of two active domains and a single 100 amino acid fragment does not relate the information necessary to describe the structures within SEQ ID NO: 2 that are indispensable to its function, because a mistake of even a single amino acid can easily abolish function. Applicants disclosure does not provide this level of detail.

Finally, applicants argue that the specification provides numerous assays for determining which fragment would have activity. However, the instant rejection is a 35 U.S.C. § 112 first paragraph written description rejection, not a rejection under 35 U.S.C. § 112 first paragraph enablement, where undue experimentation is a consideration. The test for written description is

possession. An assay for finding particular claimed fragments do not equate to possession of said fragments, because such assays do not relate to one of skill the specific information that would allow one of skill to envision the other members of the claimed genus. The rejection is maintained.

The instant written description rejection is also directed to that element of the claims drawn to the use of the present methods in finding modulators of tumorigenesis. However, these arguments have not been responded to. It was maintained in the first action on the merits mailed February 13, 2004 that applicants have provided no teaching of how any function of 47169 activity is responsible for or causes tumorigenesis, and further, that the prior art appears to be silent on such a relationship. Therefore, applicants are not considered to be in possession of methods of modulating tumorigenesis comprising comprising screening for modulators of 47169 activity. Although applicants briefly refer to this rejection while arguing for enablement, there are no arguments provided for how the specification supports such a connection, and therefore the rejection is maintained.

Claims 27, and 29-31, and new claims 36-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, and is repeated for the same reasons of record as cited in the action mailed February 13, 2004.

Applicants assert that the specification provides all of the necessary teachings to enable one of skill in the art to carry out the claimed invention, because the specification supplies a list

of candidate compounds and numerous cell based assays that can be used to determine an effect on tumorigenesis.

It is accepted that applicants disclose a list of potential compounds that may be used for screening, along with a lengthy list of assays that one can carry out on the claimed protein, SEQ ID NO: 2. However, nowhere, in any of applicants specification or arguments to date, to applicants indicate that the protein of SEQ ID NO: 2 has ever been shown to be involved in any disease process related to tumorigenesis. Therefore, despite the presence of numerous compounds and assays, without such any connection established between SEQ ID NO: 2 and tumorigenesis other than the instant claim language the instant methods of screening for inhibitors of tumorigenesis is nothing more than hypothetical. It is axiomatic that treatments of any kind must be developed with assays using model systems that replicate the diseased condition. Without such a connection, there can be no predictability to finding such inhibitors, which would force the skilled artisan to perform undue trial and error experimentation to find any modulator of tumorigenesis. The rejection is thus maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 27, 29-31, and 36-42 are rejected under 35 U.S.C. 102(b) as being anticipate by Russell et al.

At the outset it is reiterated that the instant claims do not require anything from SEQ ID NO: 2 other than its presence in the tested composition.

The claims of the instant invention are drawn to a method of screening for modulators of tumorigenesis comprising adding a test compound to a first composition comprising a polypeptide of SEQ ID NO: 2, and comparing the activity of SEQ ID NO: 2 in this composition to that of a second composition that is identical to the first composition except no test compound has been added, whereby a compound is selected that is useful for modulating tumorigenesis. The invention is also drawn to the above whereby SEQ ID NO: 2 transfers an N-acetylglucosamine moiety from uridinde disphosphate to a hyudroxyl moiety of a serine or threonine residue of a protein, or wherein the composition is in a cell, or wherein the test compound is selected from the group consisting of an antibody, a small molecule, or a peptide, or where the polypeptide comprises heterologous sequences, or wherein the cell is a colon cell, an ovarian cell, a breast cell, a lung cell or a liver cell.

Russell et al. teaches a method of screening for modulators of prostate tumorigenesis. Although Russell et al. is silent as to SEQ ID NO: 2, the instant specification teaches that SEQ ID NO: is expressed in prostate cells, and therefore, SEQ ID NO: 2 is considered inherent to the teachings of Russell et al. Accordingly, Russell et al. is also considered to teach such screening methods comprising compositions comprising SEQ ID NO: 2 whereby an N-acetylglucosamine moiety is transferred from uridinde disphosphate to a hyudroxyl moiety of a serine or threonine residue of a protein, and wherein the composition is in a cell, and wherein the test compound is selected from the group consisting of an antibody, a small molecule, or a peptide, or where the polypeptide comprises heterologous sequences, and wherein the cell is a colon cell.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz, Ph.D. whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JD Schultz, PhD